(FILE 'HOME' ENTERED AT 17:19:02 ON 02 FEB 2004)

FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:19:22 ON 02 FEB 2004

L1	246830	S	BINDING PAIR OR (AVIDIN AND BIOTIN) OR (LIGAND AND (ANTI-LIGA
L2	156004	S	COLLOID OR LIPOSOME OR CATIONIC LIPID OR CATIONIC AMPHIPHILE
L3	127513	S	((POLYMER OR POLYMERIC) AND MATRIX) OR MICROSPHERE OR MICROPA
L4	280958	S	L3 OR L2
L5	1475	S	L4 AND L1
L6	934		DUP REM L5 (541 DUPLICATES REMOVED)
L7	1098384	S	CONJUGATED OR COMPLEXED OR BOUND
L8	269	S	L7 AND L6
L9	173	S	L8 NOT L3
L10	11059336	S	THERAP? OR IMAGING OR DIAGNOS?
L11	62	S	L10 AND L9
L12	95	S	L8 AND (BIOTIN AND AVIDIN)
L13	95		DUP REM L12 (0 DUPLICATES REMOVED)

L13 ANSWER 53 OF 95 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN 1996-03360 BIOTECHDS
TI Solid **microparticle** for gene delivery to specific cells; with gelatin and crosslinked **avidin**, hormone, antibody, cell adhesion molecule, saccharide, drug or neurotransmitter for use in **receptor**-mediated gene transfer and gene therapy
AU Truong V L; August T; Leong K W
PA Univ.Johns-Hopkins
LO Baltimore, MD, USA.
PI WO 9600295 4 Jan 1996
AI WO 1995-US7857 23 Jun 1995
PRAI US 1994-265966 27 Jun 1994
DT Patent
LA English
OS WPI: 1996-068879 [07]
AB A new solid **microparticle** for gene delivery to specific target cells contains a cationic polymer and nucleic acid (DNA or RNA at 5-20%, e.g. a gene of at least 10 kb), with a linking molecule or targeting **ligand** attached to the **microparticle** surface. The linking molecule (e.g. **avidin**) may be attached via glutaraldehyde crosslinking. The targeting **ligand** may be a hormone, antibody, cell adhesion molecule, saccharide, drug or neurotransmitter. The cationic polymer may be gelatin. A biotinylated targeting **ligand**, e.g. with **biotin bound** to an antibody at oligosaccharide groups on the Fc portion, may be coupled to the linking molecule. The particle may also contain chondroitin sulfate. The particles may be formed by coacervation of nucleic acid to the cationic polymer, allowing the linking molecule or targeting **ligand** to adhere to the surface, and optionally crosslinking the linking molecule or target molecule to the **microparticle**. At the coacervation step, 2-7% gelatin, 1-500 ug/ml nucleic acid and 7-43 mM sodium sulfate are present. The method allows e.g. **receptor**-mediated gene transfer or gene therapy. (33pp)

for linkage to a biological or chemical agent (I); (15) an article comprising a **colloid** particle immobilized relative to a glutathione derivative and at least one signaling entity; (16) an article comprising a **colloid** particle carrying on its surface, a self-assembled monolayer comprising a glutathione derivative.

USE - Methods, compositions, species and articles for detecting or monitoring interactions between chemical and biochemical species, including drug screening assays, are provided. For detecting interactions between ligands and target receptors on the surface of live intact cells to enable screening of candidate compounds which disrupt these interactions. For screening compound libraries for drugs that inhibit the activity of cell surface receptors. For examining e.g. protein/protein, protein/peptide, antibody/antigen, antibody/hapten, enzyme/substrate, enzyme/inhibitor, enzyme/cofactor, binding protein/substrate, carrier protein/substrate, lectin/carbohydrate, **receptor**/hormone, **receptor**/effector, complementary strands of nucleic acid, protein/nucleic acid, repressor/inducer, **ligand**/cell surface **receptor** and virus/**ligand** interactions. For identifying cell-derived molecules (e.g. receptors or proteins), that are expressed differentially in healthy versus diseased tissue or cells, i.e. **diagnostic** assays for determination of diseased states. For visually investigating patterns of cell surface **receptor** expression on individual cell surfaces and/or on cells embedded in a tissue specimen. Biospecific colloids (gold colloids) may be used to facilitate in vivo **imaging**, e.g. detection of tumor using X-ray or X-ray computer tomography.

ADVANTAGE - A series of components and techniques for drug screening are provided. The approach provides: (I) modular system for the attachment of natural ligands to universal signaling elements; (ii) enhanced sensitivity of detection through the attachment of a plurality of signaling elements to each **ligand**; (iii) a simpler format (without the need for washing steps, enzymatic cleavage and toxic substrates); (iv) a convenient electronic output; and (v) the capability of multiplexing. Further advantages over existing methods such as ELISA, fluorescent labeling and SPR include: in the above systems, there is no need for protein labeling; the protein is attached to a labeled component. Gold colloids can be pre-labeled with both: (a3) a signaling moiety; and (b3) a functional group for protein attachment. Self assembled monolayers that present both NTA/Ni2+, to capture histidine-tagged proteins, and a ferrocene derivative, for electronic or electrochemical signaling, can be formed on the colloids. SAMs that incorporate carboxylic acid groups, for the chemical coupling (standard EDC/NHS chemistry) of unmodified proteins, can also be used. Virtually any biological species can be co-immobilized on colloids with a signaling entity. The technology enables cost-effective multiplexing as it can readily be multiplexed on microelectrode arrays. (NTA = nitrilo triacetic acid; SAM = self-assembled monolayer).

EXAMPLE - A target protein, Glutathione-S-Transferase (GST) was histidine-tagged and immobilized on SAM-coated colloids that presented NTA-Ni (histamine tags bind NTA-Ni). 30 microl of colloids presenting 40 microM NTA-Ni on the surface were added to 65 microl of 21.5 microM GST, to give a final concentration of 14 microM GST in solution. Glutathione, a small molecule that binds GST, is commercially available **bound** to agarose beads through Sigma-Aldrich. Glutathione-coated beads were incubated with the solution of GST-**bound** colloids. Within minutes, the GST **bound** to the glutathione beads, bringing the colored colloids out of solution, and decorating the beads red (Figure 20). Beads displaying a small molecule that does not bind to GST remained colorless when incubated with the GST-**bound** colloids (Figure 21). A second negative control, in which glutathione-coated beads were incubated with 30 microl NTA-Ni colloids in the absence of GST showed that NTA-Ni-colloids do not bind nonspecifically to the bead surfaces or to the glutathione. (83 pages)

L11 ANSWER 33 OF 62 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN 2002-10819 BIOTECHDS
TI Interaction of species (e.g. biological **ligand**) immobilized on colloidal particles, with species (e.g. molecule capable of reacting with **ligand**) immobilized on non-colloidal structure e.g. magnetic beads, useful in e.g. drug screening;
biological **ligand** interaction, **colloid** particle immobilization and magnetic bead, for drug screening
AU BAMDAD C C; BAMDAD R S
PA MINERVA BIOTECHNOLOGIES CORP
PI WO 2002001228 3 Jan 2002
AI WO 2000-US20168 23 Jun 2000
PRAI US 2000-602778 23 Jun 2000
DT Patent
LA English
OS WPI: 2002-205935 [26]
AB DERWENT ABSTRACT:
NOVELTY - (1) A method comprises allowing a **colloid** particle the ability to become immobilized with respect to a non-colloidal structure (II); and determining immobilization of the **colloid** particle relative to (II).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (2) signaling a single binding of a first biological or chemical agent to a second biological or chemical agent with a plurality of signaling entities; (3) determining protein/**ligand** interaction in the absence of SPR without labeling either the protein or the **ligand**; (4) a method, comprising: (a) providing: (i) a solution comprising colloids, the colloids comprising a **ligand** capable of interacting with a cell surface molecule and (ii) a composition comprising an electrode comprising growing cells, the cells comprising at least one cell surface molecule capable of interacting with the **ligand**; (b) adding at least a portion of the colloids to the composition; (5) a method comprising: (a1) providing: (i) a solution comprising colloids, the colloids comprising a **ligand** capable of interacting with a cell surface molecule, (ii) a candidate drug, and (iii) a composition comprising an electrode comprising growing cells, the cells comprising at least one cell surface molecule capable of interacting with the **ligand**; and (b1) mixing at least a portion of the colloids with the drug and the composition; (6) recruiting an electronic signaling entity to an electrode using a magnetic material; (7) an article defining a surface, and a **ligand** suspected of interacting with a protein and an electroactive entity each immobilized relative to the surface; (8) an article comprising: a first biological or chemical agent, capable of biological or chemical binding to a second agent, immobilized relative to a plurality of signaling entities; (9) an article defining a surface, and a self-assembled monolayer formed on the surface of the article; (10) a composition comprising a first molecule and one or more signaling entities attached to a solid support, where the first molecule is a **ligand** capable of interacting with a cell-surface **receptor** or protein; (11) a composition, comprising a first molecule, a second molecule and a third molecule attached to a solid support, where the first molecule comprises a **ligand** capable of interacting with a cell-surface **receptor** or protein, where the second molecule forms a monolayer on the solid support, and where the third molecule is electroactive; (12) an article comprising a metal support constructed and arranged to support the growth of cells on its surface, the metal support comprising a monolayer of at least one type of molecule, the monolayer configured such that the metal support can be used as an electrode; (13) a composition comprising: a **colloid** particle; a signaling entity immobilized relative to the **colloid** particle; and a protein immobilized relative to the **colloid** particle; (14) a species comprising: a polymer or dendrimer carrying a plurality of signaling entities adapted

L11 ANSWER 47 OF 62 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93075114 EMBASE
DN 1993075114
TI Active removal of radioactivity in the blood circulation using **biotin**-bearing liposomes and **avidin** for rapid tumour **imaging**.
AU Ogihara-Umeda I.; Sasaki T.; Nishigori H.
CS Faculty of Pharmaceutical Sciences, Teikyo University, Suarashi 1091-1,Sagamiko-machi, Kanagawa 199-01, Japan
SO European Journal of Nuclear Medicine, (1993) 20/2 (170-172).
ISSN: 0340-6997 CODEN: EJNMD
CY Germany
DT Journal; Article
FS 016 Cancer
023 Nuclear Medicine
037 Drug Literature Index
LA English
SL English
AB In order to shorten the delay between the administration of tumour-**imaging** agents and obtainment of scintigrams, rapid delivery of radionuclide to tumours followed by rapid clearance from the blood is required. We used liposomes with **biotin bound** on their surface (B-liposomes) as carriers for rapid delivery. For rapid blood clearance, we employed **avidin** in the expectation that the strong affinity between **biotin** and **avidin** would result in the aggregation of B-liposomes in the blood circulation, and that these aggregates would be taken up rapidly by the reticuloendothelial system, resulting in the rapid elimination of liposomes and the radionuclide encapsulated in them. When B-liposomes encapsulating gallium-67 deferoxamine were intravenously administered to mice bearing sarcoma 180, large amounts of 67Ga were delivered to tumours by 4 h after injection, though the 67Ga blood level remained high. On the other hand, administration of **avidin** 4 h after administration of the B-liposomes dramatically reduced the blood level so that it was only 5% of that in the non-treated group 1 h later. As a result, the tumour-to-blood ratio reached nearly 14 at 5 h after radionuclide administration, suggesting that rapid tumour-**imaging** will be feasible by means of this method.

L11 ANSWER 60 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:748430 CAPLUS
DN 126:14778
TI Binding molecule complexes with two or more effector molecules, and **therapeutic** and other uses thereof
IN Virtanen, Jorma; Virtanen, Sinikka
PA Burstein Laboratories, Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9632841	A1	19961024	WO 1996-US5389	19960418
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5718915	A	19980217	US 1995-424874	19950419
	AU 9655554	A1	19961107	AU 1996-55554	19960418
	JP 2002503945	T2	20020205	JP 1996-531913	19960418
PRAI	US 1995-424874	A	19950419		
	US 1994-332514	A2	19941031		
	US 1996-627695	A	19960329		
	WO 1996-US5389	W	19960418		

AB Structures that bind to a selected target are prepd. having two or more different effector mols. joined to each other by a joining component. At least one of the effector mols. (e.g. an antibody) binds to the target and at least one of the other effector mols. (e.g. an enzyme) is **therapeutic**. The joining component may be a **liposome**, protein, dendrimer polymer or complementary nucleic acid chains. The joining component may be of sufficient length and/or flexibility to permit the **therapeutic** mol. to phys. interact with the target at the same time as the binding mol. binds with the target. The structures may be used in disease treatment, immunoassays and sensors. For in vivo genetic manipulation of cells, the **liposome** joining component is filled with a plurality of genetic manipulation complexes that contain a polynucleotide having a sequence for recombination and a binding site, a DNA binding protein **bound** to the binding site and a motor protein **conjugated** to the polynucleotide. Prophospholipase may be on the surface of the **liposome**, and when activated cleaves the **liposome** to release the complex.